

Appln No.: 09/824,587  
Amendment Dated: January 11, 2004  
Reply to Office Action of October 31, 2003

#### REMARKS/ARGUMENTS

This is in response to the Office Action mailed October 31, 2003 for the above-captioned application. Reconsideration and further examination are respectfully requested.

In response to the Examiner's comments concerning claim numbering and to assure clarity, Applicants are including a complete set of the pending claims (21-54). None of these claims are amended at this time. The listing of claims indicates that claims 19 and 20 are cancelled.

The Examiner rejected claims 48-50, stating that it was unclear if the hybridoma cell lines referenced in the claims had been deposited and were publicly available. Applicants advise the Examiner that the hybridoma's, which were deposited with the European Collection of Cell Cultures and assigned the indicated numbers are publicly available and have been publicly available since the publication of the European Application.

Claims 21-23, 29, 35-38 and 44-47 stand rejected as anticipated by US Patent No. 4,900,662. Applicants respectfully traverse this rejection. For anticipation to be proper, the reference relied upon must teach each and every element of the claimed invention. This is not the case in this instance. In particular, while Shah discloses several of the individual steps, they are not used in the same manner as in the present invention. For example, Shah may make sandwich in the form: antiA-A-antiA-support, but the reference does not teaching making this sandwich in both a simultaneous and stepwise fashion and then comparing the results. Furthermore, for the two antigens, the first and second binding agents used by Shah are the same for a given antigen, but different for each antigen. In the claimed invention, the binding reagents are the same in each assay, but different from one another. In view of the foregoing differences, Applicants submit that the rejection for anticipation based on Shah should be withdrawn.

Claims 24-28, 30-34 and 39-43 stand rejected under 35 USC § 103 as obvious over the combination of the Shah patent and Creus. The Examiner acknowledges that the Shah reference does not teach measurement of gonadotrophic hormones such as FSH, but that it would have been obvious to use Shah's techniques to measure FSH, the hormone measured in Creus.

As a first matter, this rejection is flawed because Shah, as explained above, does not actually teach the methodology claimed in this application. Thus, even if the Examiner's combination of the references is appropriate, the result would not be a method as claimed in this application. Applicants further submit, however, that the Examiner has failed to provide a reason separate from Applicants disclosure, for the proposed combination of references.

The law is well established that "obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or

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incentive supporting the combination." *Carella v. Starlight Archery and Pro Line Co.*, 804 F.2d 135, 140, 231 USPQ 644, 647 (Fed. Cir. 1986) (citing *ACS Hosp. Syss., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984)). "[T]he factual inquiry whether to combine references must be thorough and searching." *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1351-52, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). This factual question cannot "be resolved on subjective belief and unknown authority," *In re Lee*, 277 F.3d 1338, 1343-44, 61 USPQ2d 1430, 1434 (Fed. Cir. 2002); "it must be based on objective evidence of record." *Id.* at 1343, 61 USPQ2d at 1434. Furthermore, the mere fact that teachings found in the prior art **could** be combined as proposed by an examiner does not make the combination obvious "absent some teaching, suggestion or incentive supporting the combination." *Carella*, 804 F.2d at 140, 231 USPQ at 647 (citing *ACS Hosp. Syss., Inc.*, 732 F.2d at 1577, 221 USPQ at 933).

Shah and Creus have no relation to each other beyond the fact that teaches detection of materials in humans. The Shah patent relates to the detection of isoforms of an **enzyme** creatinine kinase that are indicative of the recent occurrence of myocardial infarction. There is no mention in the Shah patent that the assay methodology is applicable to other materials in general, and no mention of FSH or other gonadotropins. Creus relates to FSH isoforms, and their different activity levels in post-menopausal and menstruating women. Creus has nothing to due with myocardial infarction. Thus, the only thing linking these two documents is the present invention, not a teaching or suggestion found in the art.

The Examiner states that one skilled in the art would be motivated to use the Shah technique to measure FSH isoforms "because Shah discloses that diagnosis of acute disease is often based on abnormal levels of disease markers such as hormones in biological fluids." Applicants respectfully point out that neither menopause nor menstruation is a "disease" nor an "acute disease." Thus, this passage from Shah in no way directs one skilled in the art to apply Shah's teachings in the context of measuring FSH. Furthermore, the Examiner states that Shah's techniques are beneficial when the level of the marker "changes momentarily during the acute phase" but has not shown that this condition is met in the case of FSH in post-menopausal or menstruating women.

Finally, the Examiner states that "Creus teaches [that] a woman's endocrine status affect (sic) the circulating FSH isoforms" and that "therefore a complete evaluation of FSH using immunoassays as taught by Shah would have been desirable and convenient with the use of antibodies." Creus teaches the existence of multiple isoforms of FSH, but does not teach antibodies that are selective for these isoforms, nor provide any assurance that selective antibodies can be obtained. Selective and non-selective antibodies are both used in Shah's method however. (Page 6, lines 29-34). Thus, there is no teaching of elements necessary to enable the supposedly obvious invention, nor even a reasonable expectation of success.

For these reasons, the rejection under 35 USC § 103 should be withdrawn.

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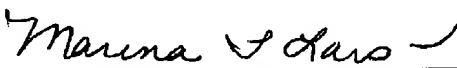
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The Examiner also provisionally rejected claims 21-50 for obviousness-type double patenting over claims 18-22 and 26-28 of copending application 09/828,624. Applicants respectfully submit that this rejection is in error. In making this rejection, the Examiner has stated that the claims in the two application are obvious because they relate to methods for accomplishing the same result. This is not sufficient to support this rejection. The steps used to accomplish the result must be obvious or trivial variants one over the other. Since the steps are not similar, and in particular since the type of assays are different, this rejection is in error.

Specifically, in the present application, the method for differentiating between a first state and a second state involves performing two separate assays that form antibody-analyte-antibody sandwiches, one of which is performed in a stepwise manner, and the other which is performed with all reagents present at substantially the same time. In these claims, the same antibodies are used in each test. In contrast, in the '624 application, the claims are directed to an assay methodology in which contemporaneous first and second assays are performed on a sample. The first assay uses a first set of reagents and produces an indication of the gonadotropin that is independent of the whether the individual is pre- or post-menopausal. The second assay uses a second, and different set of reagents, and produces an indication of the gonadotropin that differs depending on whether the human female individual is pre-menopausal or post-menopausal. Thus the actual method steps do not overlap and are not obvious variants of one another. Accordingly, the double-patenting rejection should be withdrawn.

For these reasons, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully Submitted,



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